|  |  |  |
| --- | --- | --- |
| PROTOZOA: | ***Trypanosomiasis (brucei gambiense/rhodesiense)*** | Trypanosomiasis cruzi |
| **English Name** | African Trypanosomiasis, “Sleeping Sickness”, Nagana Disease | American Trypanosomiasis; Chagas Dz |
| **Mode of transmission and the infective form** | Extracellular flagellated (runs along its length) protozoa (trypomastigote) spread by  **Tsetse Fly** bite | Intracellular flagellated (runs along its entire length) protozoa (trypomastigote) spread by  **Reduviid bug** (Rhodnius, Triatoma, and Panstrongylus genera= “kissing bug”; “assasin bug”) bite  Also eating uncooked food with contaminated feces (mucosal entry); blood transfusion/transplants; labs  Also transplacental or during delivery, or while breastfeeding  Occupational exposure (research) |
| **Life Cycle** | * Indirect Life Cycle * **Tsetse Fly**: injests trypomastigotes from human blood🡪Lives in gut. Tsetse fly injects metacyclic trypomastigotes into humans * **Human**: Replicates in blood and travels in blood and lymph🡪tsetse fly takes blood meal   **Reservoir:** Wild animals | * Indirect Life Cycle * **Reduviid bug. Protozoan** lives in gut of reduviid as epimastigotes. Bug lands on host and transmits protozoan through bite or its feces (when its eating its pooping and gets into host when host scratches). 🡪 * **Human**: invade blood stream and lymphatics 🡪 infects tissue (predilection for striated muscle including the heart)🡪 replicate in tissue as amastigotes🡪 evolve into trypomastigoes and rupture into blood   Direct correlation btw infected wild-animal reservoir hosts and the presence of infected bug nests in human homes🡪zoonosis |
| **Migration w/in Humans** | * Trypomastigotes replicate by binary fission in various body fluids; blood, lymph, CSF and meninges | * Trypomastigotes invade various cells at site of infection 🡪 morph into amastigotes * Amastigotes replicate by binary fission in the body tissues 🡪 morph into trypomastigotes 🡪 released into blood * Invade more tissues, cycle repeats |
| **How is pathology produced?** | * Surface trypanosomiasis has antigenic (VSG) variable surface glycoprotein🡪 diff VSG’s are expressed by organisms w/in a pop🡪 replacement pop to be generated after effective Ab response against the dominant VSG🡪 evasion of response   **W. African Sleeping Sickness**   * *T.b. gambiense* * IP: few days to weeks * Initially an inflamed nodule @ bite site🡪spreads to lymph nodes 🡪 When in neck area get **Winterbottom sign—inflammed L.N.**    + Screen Shot 2012-11-05 at 10 * Fever (febrile episodes may last years), rash, edema, myalgia, arthralgia 🡪 then inflammation of the CNS (causing sleeping sickness) * CNS involvement: lethargy, tremors, meningoencephalitis * Final stages of dz—hemiplegia, incontinence, coma, death   **E. African Sleeping Sickness**   * *T.b rhodesiense* * Similar to above, but shorter incubation & more virulent, severe, and fatal. * Acute Dz: fever, rigors, and myalgia. Progresses rapidly—death w/in 12 mo if untx * Develops in greater #’s in the blood * Lymphadenopathy is uncommon—**no winterbottom sign** * CNS invasion occurs early in infection   **3 stages of infection**   1. **Chancre** (may dev @ inoculation site)🡪 **hemolymphatic** stage (fever, lymphadenopathy, and pruritis)🡪 **meningoencephalic** stage (invasion of CNS causing headaches, somnolence, abn behavior, and leading to loss of consciousness and coma) | * Asymptomatic, acute, or chronic * Early sign: Chagoma: erythematous & indurated area at site of bite * Followed by rash/edema around eyes and face (**Romaña’s Sign)** * Acute: * Most common and severe in children <5 * Usually CNS involved * Fever, chills, myalgia, malaise, fatigue (flu like) * Death after few weeks (congestive heart failure) OR recovery OR…chronic phase * Chronic: * Proliferation and spread to viscera * 30% develop “mega-syndrome” (even over 10 yrs post infection): myocarditis, dilated cardiomyopathy, enlargement of esophagus & colon b/c dead nerve cells don’t control growth. * Major cause of cardiomyopathy (mega-cardio) in Central and S. America * Involvement of the CNS may produce granulomas in the brain🡪 cyst formation, meningoencephalitis |
| **Diagnosis –** What sample? What is seen? | * Thick and thin Blood smears, lymph aspirations, CSF may all show extracellular flagellated protozoans (larger than RBC) * Description: Trypansoma brucei sp in a thin blood smear, dividing * Winterbottom Sign: swollen lymph nodes on posterior neck * Serology * PCR (not routine) to detect infections and to diff species | * Acute: thick and thin blood smear should show parasites * Chronic: organisms leave blood and are hard to find, so use biopsy of LN, liver, spleen, or bone marrow and look for amastigotes * + T. cruzi trypomatigoes in blood (L pic)   + Amastigotes persistent inside cells (R pic) * Xenodiagnosis (endemic areas): Serology, PCR   + Take uninfected vector (reduviid) and allow to feed on suspecting host🡪 then try and recover parasite from vector after a few weeks |
| **Definitive host** | Humans and Hoofed Mammals | Humans and Hoofed Mammals |
| **Intermediate host(s)** | Tsetse Fly | Reduviid Bug |
| **Form transmitted from human to next host** | Trypomastigote | Trypomastigote |
| **Geographical foci** | *T.b. brucei gambiense*: Tropical West & Central Africa  *T.b. rhodesiense*: East Africa esp in cattle raising countries | North, Central and South America (most important vector borne dz in latin America), A lot in Southern U.S.A. (Arizona) |
| **Treatment/Prevention** | * Suramin (does not cross BBB) * Pentamidine (alternative)—also doesn't cross BBB * Melarsoprol for CNS involvement in rhodensciense * Eflornithine for CNS involvement in Gambian * No vaccine | * Nifurtimox or Benznidazol for acute phase (these are toxic) * No drugs effective against chronic dz—maybe benznidazol * No vaccine |

* Merozoites have a "signet-ring" appearance due to a large vacuole that forces the parasite’s nucleus to one pole
* Schizonts are round to oval inclusions that contain the deeply staining merozoites
* Gametocytes are 'halter-shaped' similar to *Haemoproteus* but the pigment granules are more confined

|  |  |  |
| --- | --- | --- |
| **PROTOZOA:** | ***Plasmodium (falciparum, vivax, ovale, & malariae)*** | Leishmania donovani |
| **English Name** | Malaria | Leishmaniasis |
| **Mode of transmission and the infective form** | Spread by female *Anopheles* mosquito carrying sporozoites  Also blood transfusion, IV needles, or congenital | * Spread by ***phlobotomine* sand flies** (vector) carrying the promastigote   + usually zoonotic from a wild-animal reservoir (small rodents, dogs, cats); can also be anthroponiotic from an infected human host * Also direct contact with lesions; mechanically by stable flies; or sharing needles * Dimorphic   + adult (flagellated-**infective** form); free promastigote in vector (sand fly)   + obligate intracellular amastigote (non-flagellated) in mammalian definitive hosts (divide w/in macrophages)🡪 **diagnostic form** |
| **Life Cycle** | * Indirect life cycle * **Mosquito**: Gametes 🡪 sporozoites (in salivary gland) * **Human**: Sporozoites 🡪 go to liver and form schizonts 🡪 leave hepatocytes and release merozoites which infect RBCs | * Flagellated free promastigote in vector egested into host * Promastigotes (flagellated & extracell) are phagocytosed by macrophages; morph into amastigotes (no flagella & intracell) inside the macrophage🡪amastigotes multiple in cells 🡪 macrophage w/ amastigote taken up by sand fly during blood meal |
| **Migration w/in Humans** | * Egestion of sporozoites from mosquito 🡪 hepatocytes * Hepatocytes release merozoites 🡪 RBCs (chronic) * Form gametocytes 🡪 Sucked up by mosquitos | * Egestion of promastigotes from mosquito into human blood * Taken up by macrophages, spread to various tissues |
| **How is pathology produced?** | * Lysing of RBCs by the merozoite stage. * *Vivax* * immature RBC’s w/ **Duffy Ag**   + - Duffy Ag is a chemokine receptor used by vivax merozoites to enter RBC’s     - So if you lack the Duffy Ag you are resistant to P. vivax * Relatively benign; “flu-like” symptoms * Can be dormant in liver (hipnozoites) and relapse even after blood is cleared of merozoites * Travelers can exhibit disease years after infection * Incubation: 10-17 days * Most untx’d patients can survive but can relapse * *Ovale*: Similar to P. vivax * immature RBC’s BUT NO duffy ag use * *Malariae*: mature RBC’s * No large RBC with parasites b/c mature RBC have more rigid membrane * **No** liver involvement 🡪 no relapses * Longest incubation—18-40 days * Untreated infections can last many years * *Falciparum*: infects any age RBC’s * Causes vast majority of malarial deaths * **No** liver involvement 🡪 no relapses * Shortest incubation—7-10 days * Untx disease🡪 malignant tertian malaria * Daily chills, fever, N/V/D, dehydration * Anemia (due to ↑ inflamm & hemolysis🡪 can lead to toxic cellular debris) * Generates and inserts PfEMP1 adhesive protein into RBC membranes which causes the RBC to be sticky🡪 PfEMP1 can bind to host receptors; clogs capillaries by binding platelets/other RBCs (“rosetting”)🡪 can help evade spleen dependent killing by sequestration * PfEMP1 also causes Antigenic variation to evade Ab defenses * Capillary “plugging” due to PfEMP1 results in cerebral/placental malaria * Hemolysis and obstruction of renal capillaries results in renal failure * Clogging of capillaries can result in hepatic and lung pathology * Sickle cell anemia hetero’s (HbAS) are protected | * **Visceral leishmaniasis (kala-azar**): multi-organ infection; AIDS opportunist * ***L. donovani; L. infantum*** * Opportunistic in AIDS pts * Most serious🡪multi organ infection—grows in macrophages * Fatal, chronic, or even asymptomatic & self limiting * Reticulo-endothelial system invasion 🡪 enlarged L.N., spleen & liver * Fever, rigor, chills often intermittent * fatigue & weakness (due to anemia-persistent inflammation and hypersplenism🡪 ↑ in RBC destruction) * **Cutaneous leishmaniasis**: ulcerative, skin disfiguring infection * 1st Red pruritic papule @ site of fly’s bite🡪 gets itchy, irritated and begins to enlarge/ulcerate 🡪 skin disfigured (slow healing) * 2o infection common🡪 skin disfiguring infection (slow healing usually leaving disfiguring scar) * 90% are in Afgan., Brazil, Iran, Peru, Saudi Arabia & Syria; focal areas in S. America * Seen in US military personnel in endemic areas * **Mucocutaneous leishmaniasis**: destruction of mucous membranes & related tissues * ***L. braziliensis***; uncommon disease   + Mostly in S. and Central America * Initially cutaneous (does not heal) 🡪 if untx’d 80% progresses (even years later) to MCL 🡪 often oral/nasal mucosae🡪w/damage to nearby structures (palate, nasal cartilage) * 2o infection common🡪 severe mutilation |
| **Diagnosis –** What sample? What is seen? | * Peripheral Blood smear for malarial forms * *Vivax*: single ring forms (immature trophozoite in RBC), or swollen RBC w/up to 24 merozoites * *Vivax/Ovale*: Schüffner's dots visible with Giemsa stain   + - Screen Shot 2012-11-02 at 12 * *Falciparum*: multiple ring forms (immature trophozoites in RBC); possibility of mixed infection with P. vivax * Crescent-shaped gametocytes are dx * Ab testing (some cross-reactivity) * PCR test for malaria genome | * Clinical presentation * Most common: detection of amastigotes (nonflagellated form) in macrophages * Molecular detection methods (most accurate, not common)—PCR for parasite DNA * MCL/CL: amastigotes in clinical specimens from skin/mucous or promastigotes in culture from ulcer tissues * VL: amastigotes in biopsy samples (splenicpuncture, LN aspirates, liver bx, sternal aspirates, iliac crest BM, & buffy coat preps of venous blood)   Cutaneus Visceral |
| **Definitive host** | Mosquito Vector | Mammals/Humans |
| **Intermediate host(s)** | Human | Sandflys (Phlebotomus and Lutzomyia) |
| **Form transmitted from human 🡪 host** | Gametes | Amastigote (in macrophage) ingested by mosquito |
| **Geographical foci** | In general—Africa, SE Asia, S. America, Central America & The Carribean  *Falciparum--*Tropical and subtropical | * 88 countries in 5 continents: Africa, Asia, Europe, N. America, and S. America * **Visceral**: Bangladesh, Brazil, India, Nepal, Sudan * **Cutaneous**: Afghanistan, Brazil, Iran, Peru, Saudi Arabia, Syria (also Brazil, Peru) * **Mucocutaneous**: Bolivia, Brazil, Peru, Central America |
| **Treatment/Prevention** | * *Vivax🡪* use chloroquin and follow with primaquin to eliminate the hipnozoites * *Falciparum* – chloroquin in areas w/o resistance; * quinine sulfate + doxy, clindamycin * atovaquone-proguanile (malarone) * Methloquine-toxic * Primaquine for hypnozoites * No vaccine—but there is a vaccine in phase III trials | * IV antimony compounds (sodium stibogluconate) * Paramomycin (antibiotic) * F/u w/ smears, cultures and/or PCR to ensure tx is working |

|  |  |  |  |  |  |
| --- | --- | --- | --- | --- | --- |
| **PROTOZOA:** | ***Cryptosporidium spp. (hominis & parvum)*** | Trichomonas vaginalis | Giardia duodenalis (lamblia or Intestinalis) | Toxoplasma gondii | ***Entamoeba histolytica*** |
| **English Name** |  | Trichomoniasis | Giardiasis | Toxoplasmosis | Amebic Dysentery |
| **Mode of transmission and the infective form** | Oocysts are ingested Fecal-oral, oral-anal | Flagellated extracellular protozoan infects genital tract via FUCKING!! (most common non-viral STD)  Also occasionally by fomites; neonates via birth canal | Cyst is ingested; usually from unsanitized water Fecal-oral; oral-anal | Oocysts passed from feline feces; ingested by human (via food or water; or if human eats raw or undercooked meat containing tissue cysts)🡪 Tachyzoites  Also transplacentally; & via transfusions (rarely) | Cyst is ingested; usually from unsanitized water  Fecal-oral; oral-anal  Also sexual transmission🡪 cutaneous amebiasis |
| **Life Cycle** | * Direct Life Cycle * Humans eat shit/cyst, shit out more cysts, eat shit/cysts again | * Direct Cycle | * Direct Life Cycle * Humans eat shit/cyst, shit out more cysts, eat shit/cysts again | * Indirect Life Cycle * **Cat**: Oocysts in cat feces. Must mature in soil before it becomes infective! * **Human**: Ingest Oocysts 🡪 Tachyzoites 🡪 Bradyzoites | * Direct Life Cycle (can be indirect via flies/cockroaches) * Humans eat shit/cyst, shit out more cysts, eat shit/cysts again |
| **Migration w/in Humans** | * Oocysts are ingested 🡪 * Develop into trophozoites in G.I. lumen * Enter into enterocyte cytoplasm (intracellular) | * Stays in genital tract of men and women | * Flagellated trophozoites grow in gut | * Oozites mature into tachyzoites, which infect muscle and neural cells (intracellular) 🡪 encyst (bradyzoites) * Also can localize to fetus in pregnant women | * Cysts ingested; stomach acid stimulates their growth into trophozoites * Trophozoites grow in gut and invade tissues & blood stream (trophozoites *not* infectious) * Cysts released in feces |
| **How is pathology produced?** | * Generally self-limiting diarrhea (watery), but much more severe in AIDS patients and can be fatal. * More common in summer months * Often asymptomatic   **Immunocompetent:**   * causes mild watery diarrhea w/o blood; spontaneously resolves   **Immunocompromised:**   * severe dehydration due to massive diarrhea; can be fatal and lasts months or years * Rarely disseminates from GI tract * Most frequent July-Aug in children   Major organs: intestinal tract (small) | * General asymptomatic or mild vaginitis or urethritis. * Never fatal * Women: commonly asymptomatic (scant, watery vaginal discharge) * Vaginal discharge (“frothy”) * Vaginitis (itching, painful urination) * Men: * Mostly asymptomatic carriers (“reservoirs” for women) * Occasionally, urethritis or prostatitis   Major Organs Affected: Urogenital tract, vagina, urethra, prostate and epididymis.  \*major cause of interfility and preterm labor in women and low birthweight in babies | * Often asymptomatic (50% carriers)🡪 can shed cysts for yrs/ IgA deficient individuals very susceptible * Causes acute intestinal sx’s including diarrhea (watery **steatorrhea--foul smelling)** which can result in chronic malabsorption * Never fatal * No tissue destruction! (mild inflammation) * Spontaneously resolves; no spread past GI   **Major organs affected**: Small intestines | **Immunocompetent:**   * Asymptomatic   **Immunocompromised** (esp. cell mediated):   * most common cause of encephalitis in AIDS patients (cysts rupture🡪 encephalitis, necrotic brain lesions seen on CT)   **Congenitally**   * Fetus: chorioretinitis (inflammation); reactivates later in life   Major organs infected: brain and eyes  \*leading cause of foodborne illness and death | * General asymptomatic or mild symptoms * Severe sx include dysentery (bloody) and spread to other organs that can be fatal (Liver abscess, less freq. in lung and brain) * Trophozoites secrete toxins and enzymes to digest human tissues * Colitis & bloody diarrhea (tissue damage) * Necrotic ulcers in mucosa * Systemic dissemination: invade blood and cause **liver**, brain and lung abscesses * Fever, leukopenia, etc (kill neutrophils!) * Immunity is Ab/complement based; T-cells important for preventing relapses * Note: most amoebae are actually commensal in humans (not this one) |
| **Diagnosis –** What sample? What is seen? | * Antibody-linked stains of stool * Oocysts are acid-fast positive * Indirect immunofluorescence assay * Detection of oocysts in feces by acid-fast staining or fluorescent staining (specific antibodies). | * Detection of parasite in from vagina urethral, prostatic secretion [trophozoites (flagellated)] no Cyst (and troph doesn’t survive in environment) * ONLY motile flagellated organism found in vaginal or urethral discharge (wet mounts) * Vaginal discharge smear 🡪 motile flagellated organism * Pap smear with fluorescent Ab stain   Trichomonas vaginalis, in vitro culture | * Microscopy/staining: trophozoite has two nucleoli & adhesive disk * Flourescent labeled cysts in stool * Detection of parasite in feces (trophozoite—flagellated/motile) and cysts      * Faces on both protozoa and cysts | * Serology for presence of *T. gondii* Ab * IgA/IgM for newborns (since mom gave IgG) * CT shows ring enhancing lesions   + [http://www.isradiology.org/tropical_deseases/tmcr/chapter45/45-10A.jpg](http://www.isradiology.org/tropical_deseases/tmcr/chapter45/large45/45-10A.jpg) | * GI: Ameba/cysts in stool (intraintestinal) or mucosal biopsy; serology (85% sensitive--extraintestinal) * Systemic: CT scan; serology (99% sensitive) * **Flask-shaped ulcers** |
| **Definitive host** | Mammals | Humans | Human and animals | Cat | Human |
| **Intermediate host(s)** | Mammals | Humans | Human and animals | Humans, mammals & birds | Human |
| **Form transmitted from human to next host** | Oocysts are released with feces into a water supply (resistant to chlorination; boil to kill)  Transmis🡪Fecal-oral (consump of oocysts), waterborne, contact w/ cattle (zoonosis) | Flagellated protozoan; STD  Transmission: Direct contact during sexual intercourse | Cyst in feces (very resistant to chlorination; boil to kill)  Transmission: fecal-oral | Tissue encysted bradyzoite  (humans normally dead-end host) | Cyst (resistant; semi-stable in environment)  Transmission: fecal-oral |
| **Geographical foci** | Worldwide | Worldwide | Worldwide  more prevalent tropical and developing countries.  In **USA, most common protozoal pathogen reported causing GI infection.** | Worldwide | Worldwide  more prevalent tropical and developing countries  **NOT** a zoonosis |
| **Treatment/Prevention** | * Supportive care mainly. * Paramomycin * Nitazoxanide (pregnant women) * anti diarrheal agents * Poor response in immunocompromised   Prevention   * Avoid fecal contamination of food or water from both human and cattle (resistant to chlorination; boil to kill) | * Metronidazole * Treat male as well to prevent relapse * Practice safe sex | * Metronidazole * Nitazoxanide (Pregnant women) * Prevention—avoid fecal contamination of food or water; boil water (kills cysts)🡪 resistant to chlorination * No vaccine | * Sulfadiazine + pirimethamine * Cook meat to 160F to kill cysts * No vaccine | * Metronidazole followed by Iodoquinol * Prevention: Avoid fecal contamination of food or water (resistant to chlorination; boil to kill) * Good hygiene * No vaccine |

**Parasites:**

* -incl primitive protozoa to arthropods
* -infect 30% humans (esp freq developing countries)
* -most infected not ill or mild sx- a dead/serverely ill host is a dead parasite
* -high combined morbidity/mortality worldwide w/ diverse immune resp

**Parasites**:

* -Protozoa (endoparasite)
* -Helminths (endoparasite)
* -Arthropods (ectoparasite)

**Hosts**:

* -final/definitive – sexually mature adult parasite (malaria mosquito; toxoplasma cat)
* -intermediate – larvae form or asexual stage of parasite
* -reservoir – harbor same species of parasites that are potential sources of human infection

**Life cycles**:

* -direct: only human host needed for entire life cycle: pinworm, hook worm, head lice
* -indirect: >1 animal host required for complete life cycle: beef tapeworm (human and ox); fluke (human and snale); malaria (human and mosquito); filariasis (human and mosquito/fly)

**Factors for transmission:**

1. source of infection: pt, carrier, reservoir host
2. Routes of transmission: congenital (toxoplasmosis), contact (direct: Trichomonas vaginalis; indir: Ascaris lumbridocdes), food, water, soil/feces, arthropod vectors
3. Suscept host: immune status, socioeconomical issues, circumstance/travel

**Effects of parasite on host**:

1. deprive essential subst
2. mechanical effect
3. toxic and allergy

**Avenues of invasion**:

1. digestive tract
2. skin
3. blood – arthropod transmission

**Prevention**: control source infection, intervention at routes, protect susceptible hosts

Epi- many people: malaria most DALYs disability adjusted life years lost (Lymphatic filariasis, Leishmaniasis, hookworm also bad)

**Protozoa:**

-simple, unicellular eukaryote

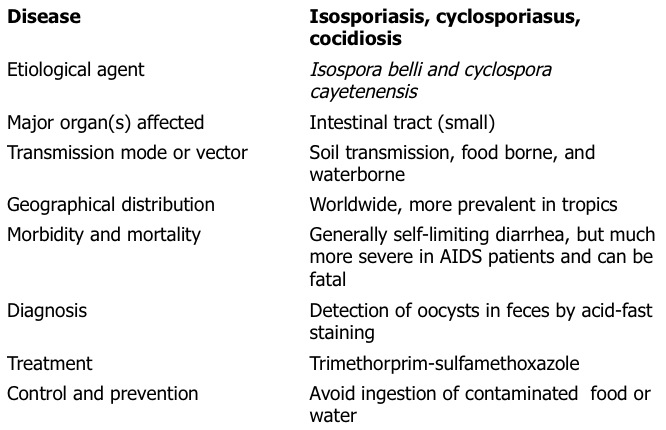
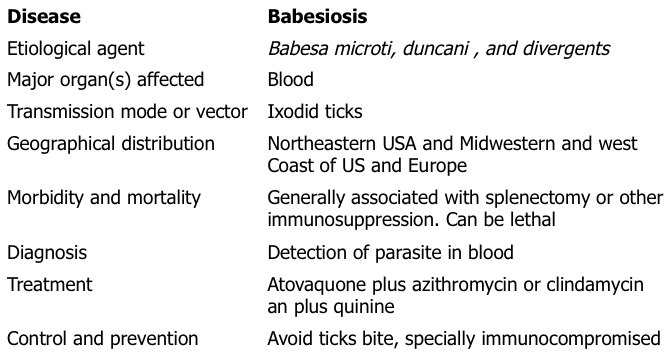
-2 forms:

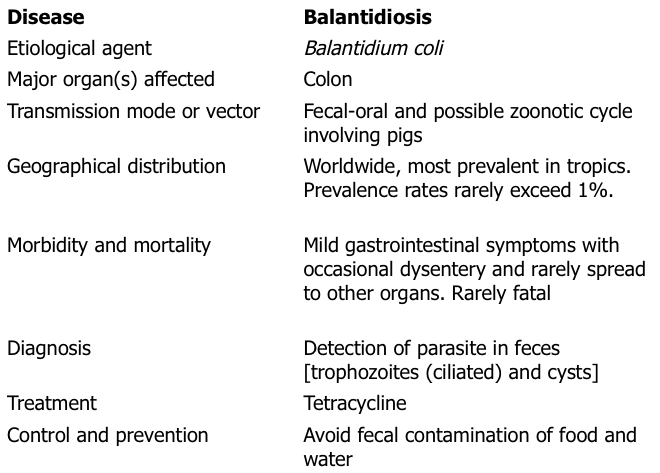
1) trophozoites: feeding and mobile stage

2) cysts: non feeding, non motile, rely on stored food

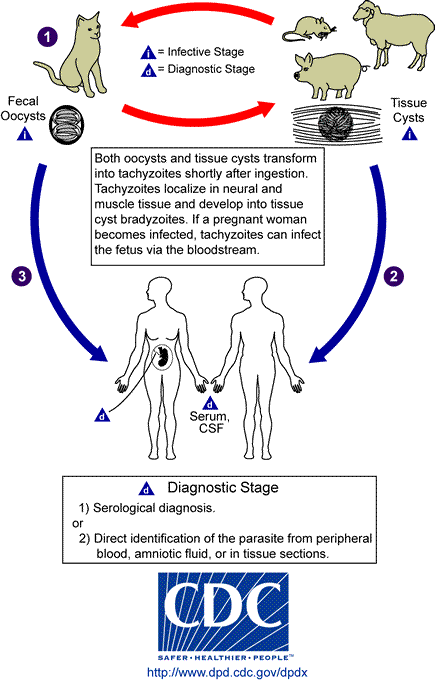
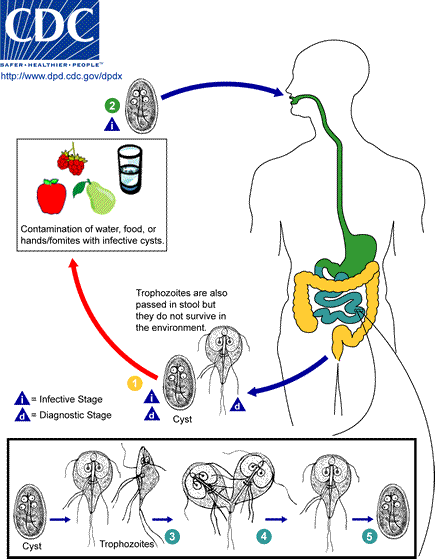
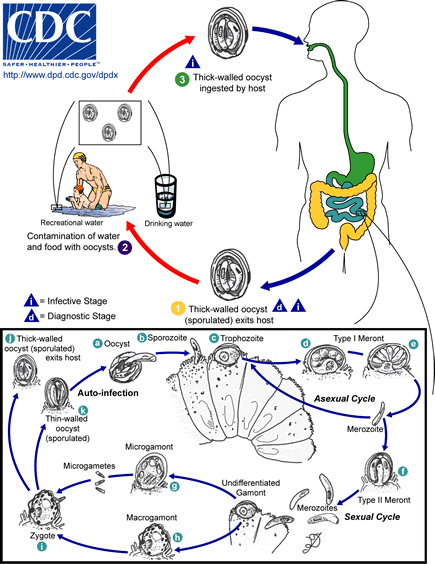
|  |  |  |  |  |
| --- | --- | --- | --- | --- |
| ANTIPROTOZOALS | | | | |
| dRUG | INDICATION | MECHANISM OF ACTION | ADVERSE EFFECTS | SPECIAL NOTES |
| Chloroquine | -**P. falciparum**/malariae treatment (sensitive species only- reports of resistance are not uncommon)  -**P. falciparum prophylaxis**  -Combination therapy w/Primaquine for other forms of malaria | -Inhibitor of heme polymerase  -causes toxic buildup of heme in erythrocytes killing erythrocytic forms | -visual disturbances  -GI upset  -**acute hemolytic anemia** (esp. G6PD) | -G6PD patients are already predisposed to hemolysis so use of this drug is potentially dangerous  -**safe in pregnancy**  -Other uses include rheumatoid arthritis & SLE |
| Primaquine | -P. vivax & ovale (kills liver **hypnozoites**)  -combination therapy w/chlroquine | -mech. Unknown  -known to be effective against **hypnozoites** far more than erythrocyte stages | -Acute hemolytic anemia (esp. G6PD)  -**DO NOT use in pregnancy** |  |
| Quinine/Quinidine | -**D.O.C. for P. falciparum (Chloroquine resistant species)**  - Combine w/pyrimethamine/sulfadoxine for Chloroquine resistant strains  -gametocidal | - According to Lange it’s unknown  -According to Clinical Micro it is a heme polymerase inhibitor | -**CINCHONISM**- broad symptom constellation including:  -Ears- Tinnitus/vertigo  -Eyes- visual disturbances  -GI-N/V/D  -CNS- headaches & fever  -Acute hemolytic anemia  -Hypotension & arrhythmias arise with IV use  -Blackwater Fever- hemolysis and hemoglobinuria associated with quinine therapy | -discontinue w/ signs of cinchonism, hypersensitivity or isolated hemolysis |
| Mefloquine | -Schizonticidal vs. P. falciparum & vivax  -ineffective vs. hypnozoites and gametocytes | -Exact Mechanism unknown | -N/V, abd pain  -reports of **psychosis** (debated)  -transaminases elevation | -Safe in pregnancy and children  -avoid w/ psych patients, cardiac patients  -DO NOT coadminister w/quinine |
| Clindamycin | -combination therapy **for P. falciparum**  -Possibly to replace doxycycline in contraindicated populations | -Binds 50s ribosomal s/u, **inhibiting protein synthesis** | -pseudomembraous colitis |  |
| Doxycycline | -**prophylaxis**  -Combination therapy for P. falciparum | - tetracycline class  -binds 30s ribosomal s/u preventing translation | -photosenstivity  -nausea  -renal & hepatic toxicity | -**DO NOT use w/ pregnancy or children**- bind calcium in developing bone/teeth |
| Pyremethamine | - **Chloroquine resistant P. falciparum** along w/quinine  -has action against all 4 malaria strains- only erythrocytic stages | -Closely related to trimethoprim  -inhibits plasmodial dihydrofolate reductase  -reduces available THF- purine synthesis cofactor | -rarely rashes, GI symptoms and itching  -severe reactions are uncommon but may include bone marrow suppression | -**Fansidar**= combination of sulfadoxine & pyremethamine  -Safe for use in pregnancy (ensure pt. is on a folate supplement) |
| Malarone (Mixture of atoqvaquone and proguanil) | -prophylaxis or treatment of P. falciparum | -Atovaquone = disrupting mitochondrial electron transport chains  -proguanil= sulfonamide class actions (against folate metabolism) | -Generally well tolerated  -may include N/V/D, abd pain, headaches or rashes but unsual with low doses | -safety in pregnancy is unknown |
| Metronidazole | -**Entamoeba histolytica**  **-Giardia lambia**  **-Trichomonas vaginalis**  **-(Anerobic bacteria & Gardenerella)** | -nitro group is reduced by susceptible species forming a toxic compound within the organism | -metallic taste  -disulfiram effect (EtOH intolerance, sorry Schmidtz) | - Don’t forget IV/Oral formulations are used to treat C. diff colitis too |
| Sodium Stibogluconate | -1st line **leishmaniasis** | -**antimonial** compound  -mechanism unknown | -increase w/duration of therapy  -GI sx, fever, rash, etc.  -ECG abnormalities may occur – Long QT and T wave abnormalities can be dangerous  -severe reactions include cardiac, renal, and hepatic toxicity (rare) | -Injection only |
| Paramomycin | -visceral leishmeniasis | -aminoglycoside class antibiotic | -injection site pain  -ototoxicity (consistent with the class)  -reversible hepatic toxicity |  |

**Other Medically Relevant Protozoa**





***Toxoplasma gondii* life cycle *Giardia sp.* life cycle *Cryptosporidium sp.* life cycle**

**--** **Oocysts passed in animal or human feces.**

***-- Cryptosporidium sp.* sporozoite infects the enterocyte itself (unlike Giardia that is outside of the cell)**

***Entamoeba histolytica* life cycle *Trichomonas vaginalis* life cycle**

**-exists only as a trophozoite**

